

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. *(currently amended)* An isolated anti-angiogenic polypeptide or peptide that is selected from the group consisting of:
 - (a) a conservative amino acid substitution variant of SEQ ID NO:5 or SEQ ID NO:6 having substantially the same transition metal ion- or plasminogen- binding activity or substantially the same biologic activity as a polypeptide of the sequence SEQ ID NO:5 or SEQ ID NO:6; and
 - (a[[b]]) a pentapeptide consensus subsequence from SEQ ID NO:5 or 6 consisting of (+) the sequence of which is (His,Pro)-(His,Pro)-Pro-His-Gly (SEQ ID NO:7), or
 - (b[[ii]]) an addition variant thereof of SEQ ID NO:7 to-in which 1 to 4 amino acids selected from His, Pro and Gly are added [[at]] to the N- or C-terminus of SEQ ID NO:7, 1 to 4 amino acids selected from His, Pro and Gly,
wherein the which pentapeptide or addition variant has substantially the same transition metal ion- or plasminogen- binding activity or substantially the same biologic activity as (i) human HPRG, (ii) rabbit HPRG, or as-(iii) a polypeptide domain of human or rabbit HPRG the sequence of which is SEQ ID NO:5 or SEQ ID NO:6, which biological activity in (a) or (b) is that of inhibiting (i) angiogenesis, (ii) endothelial cell proliferation or (iii) endothelial tube formation in an *in vitro* or *in vivo* bioassay.
2. *(currently amended)* The isolated peptide of claim 1 which is
 - (i) said pentapeptide of (b) with a wherein the sequence is selected from the group consisting of His-His-Pro-His-Gly (SEQ ID NO:8), His-Pro-Pro-His-Gly (SEQ ID NO:9), and Pro-Pro-Pro-His-Gly (SEQ ID NO:10); or
 - (ii) said addition variant of said pentapeptide wherein 1 to 4 amino acids selected from His, Pro and Gly are added at the N- or C- terminus of SEQ ID NO:8, SEQ ID NO:9 or SEQ ID NO:10.

3. (*withdrawn; currently amended*): A chemically synthesized peptide multimer comprising the pentapeptide or addition variant of claim 1, which multimer is selected from the group consisting of:

- (a) a multimer having the formula \mathbf{P}^1_n wherein
 - (i) \mathbf{P}^1 is the pentapeptide or addition variant of claim 1, and
 - (ii) $n=2-8$,
- (b) a multimer having the formula $(\mathbf{P}^1-\mathbf{X}_m)_n-\mathbf{P}^2$, wherein
 - (i) \mathbf{P}^1 and \mathbf{P}^2 are said pentapeptides or addition variants according to claim 1,
 - (ii) \mathbf{P}^1 and \mathbf{P}^2 are the same or different peptides;
 - (iii) \mathbf{X} is C_1-C_5 alkyl, C_1-C_5 alkenyl, C_1-C_5 alkynyl, C_1-C_5 polyether containing up to 4 oxygen atoms;
 - (iv) $m = 0$ or 1 ; and
 - (v) $n = 1-7$,

and wherein the peptide multimer has substantially the same ligand binding activity or biological activity as [[of]] (1) human HPRG, (2) rabbit HPRG, or (3) a polypeptide domain of human or rabbit HPRG which is SEQ ID NO:5 or SEQ ID NO:6, and which biological activity is that of inhibiting angiogenesis, endothelial cell proliferation or endothelial tube formation in an *in vitro* or *in vivo* bioassay.

4. (*withdrawn currently amended*): A recombinantly produced peptide multimer comprising the pentapeptide or addition variant of claim 1, which multimer has the formula $(\mathbf{P}^1-\mathbf{Gly}_z)_n-\mathbf{P}^2$, wherein:

- (i) \mathbf{P}^1 and \mathbf{P}^2 are the pentapeptides or addition variants according to claim 1,
- (ii) \mathbf{P}^1 and \mathbf{P}^2 are the same or different;
- (iii) $z = 0-6$; and
- (iv) $n = 1-100$,

and wherein the peptide multimer has substantially the same ligand binding activity or biological activity as [[of]] (1) human HPRG, (2) rabbit HPRG, or (3) a polypeptide domain of human or rabbit HPRG which is SEQ ID NO:5 or SEQ ID NO:6, and which biological activity is that of inhibiting angiogenesis, endothelial cell proliferation or endothelial tube formation in an *in vitro* or *in vivo* bioassay.

5. (*currently amended*) A diagnostically or therapeutically labeled anti-angiogenic polypeptide, pentapeptide or addition variant according to claim 1 or 2.

Claim 6 (Cancelled).

7. (*currently amended*) A diagnostically useful HPRG-related composition comprising:

- (a) the diagnostically labeled polypeptide or pentapeptide or addition variant of claim 5; and
- (b) a diagnostically acceptable carrier.

8. (*previously presented*) The diagnostically useful composition of claim 7 wherein polypeptide or peptide is labeled with a detectable label is selected from the group consisting of a radionuclide, a PET-imageable agent, an MRI-imageable agent, a fluorescer, a fluorogen, a chromophore, a chromogen, a phosphorescer, a chemiluminescer or a bioluminescer.

9. (*previously presented*) The diagnostically useful composition of claim 8, wherein the detectable label is a radionuclide selected from the group consisting of ^3H , ^{14}C , ^{35}S , ^{67}Ga , ^{68}Ga , ^{72}As , ^{89}Zr , ^{97}Ru , ^{99}Tc , ^{111}In , ^{123}I , ^{125}I , ^{131}I , ^{169}Yb and ^{201}Tl .

10. (*currently amended*) The diagnostically useful composition of claim[[s]] 8 wherein the detectable label is a fluorescer or fluorogen selected from the group consisting of fluorescein, rhodamine, dansyl, phycoerythrin, phycocyanin, allophycocyanin, *o*-phthaldehyde, fluorescamine, a fluorescein derivative, Oregon Green, Rhodamine Green, Rhodol Green and Texas Red.

11. (*currently amended*) : An anti-angiogenic pharmaceutical composition comprising:

- (a) the polypeptide or pentapeptide or addition variant of claim 1 or 2; and
- (b) a pharmaceutically acceptable carrier.

12. (*currently amended*): A therapeutic anti-angiogenic pharmaceutical composition comprising:

- (a) the labeled polypeptide or pentapeptide or addition variant of claim 5 to which is bound directly or indirectly a therapeutically active moiety; and
- (b) a pharmaceutically acceptable carrier.

13. (*previously presented*) The pharmaceutical composition of claim 11 [[or 12]] in a form suitable for injection.

14. (*original*) The therapeutic pharmaceutical composition of claim 12 wherein the therapeutically active moiety is a radionuclide.

15. (*original*) The therapeutic pharmaceutical composition of claim 14, wherein the radionuclide is selected from the group consisting of ^{47}Sc , ^{67}Cu , ^{90}Y , ^{109}Pd , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{199}Au , ^{211}At , ^{212}Pb and ^{217}Bi .

Claims 16 to 22 CANCELLED

23. (*withdrawn; currently amended*): A method for inhibiting cell migration, cell invasion, cell proliferation or angiogenesis, or for inducing apoptosis, comprising contacting cells associated with undesired cell migration, invasion, proliferation or angiogenesis with an effective amount of a ~~therapeutic~~-pharmaceutical composition according to claim 11.

24. (*withdrawn*): A method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis, comprising administering to the subject an effective amount of a pharmaceutical composition according to claim 11.

Claims 25 to 48 CANCELLED

49. (*currently amended*): An affinity ligand useful for binding to or isolating an HPRG-binding molecule or cells expressing [[the]] an HPRG-binding molecule, comprising a polypeptide or pentapeptide or variant according to claim 1 or 2, immobilized to a solid support or carrier.

50. (*withdrawn; currently amended*): A method for isolating a HPRG-binding molecule from a complex mixture comprising:

- (a) contacting the mixture with the affinity ligand of claim 49;
- (b) allowing any material in the mixture to bind to the ligand;
- (c) removing unbound material from the ligand; and
- (d) eluting the bound HPRG-binding molecule or cells.

51. (*withdrawn; currently amended*): A method for isolating or enriching from a cell mixture cells expressing a HPRG-binding site or receptor from a cell mixture, comprising:

- (a) contacting the cell mixture with the affinity ligand of claim 49;
- (b) allowing any cells expressing the binding site or receptor to bind to the affinity ligand;
- (c) separating cells bound to the affinity ligand compound from unbound cells; and
- (d) removing the bound cells,

thereby isolating or enriching the HPRG binding site-expressing cells.

52. (*withdrawn*): A diagnostically or therapeutically labeled peptide multimer according to claim 3 or 4.

53. (*withdrawn*): An anti-angiogenic pharmaceutical composition comprising

- (a) the peptide multimer of claim 3 or 4; and
- (b) a pharmaceutically acceptable carrier.

54. (*withdrawn; currently amended*): A therapeutic anti-angiogenic pharmaceutical composition according to claim 53, wherein comprising

- (a) ~~the peptide multimer of claim 3 or 4 to which a therapeutically active moiety is bound directly or indirectly to the peptide multimer a therapeutically active moiety; and~~
- (b) ~~a pharmaceutically acceptable carrier.~~

55. (*withdrawn; currently amended*): An affinity ligand useful for binding to or isolating an HPRG-binding molecule or cells expressing [[the]] an HPRG-binding molecule, comprising a peptide multimer according to claim 3 or 4, immobilized to a solid support or carrier.

Claims 56-57 (Cancelled).

58. (*new*) The pharmaceutical composition of claim 12 in a form suitable for injection.

59. (*new*): A method for inhibiting cell migration, cell invasion, cell proliferation or angiogenesis, or for inducing apoptosis, comprising contacting cells associated with undesired cell migration, invasion, proliferation or angiogenesis with an effective amount of a pharmaceutical composition according to claim 53.

60. (*new*): A method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis, comprising administering to the subject an effective amount of a pharmaceutical composition according to claim 53.

61. (*new*): A method for isolating a HPRG-binding molecule from a complex mixture comprising:

- (a) contacting the mixture with the affinity ligand of claim 55;
- (b) allowing any material in the mixture to bind to the ligand;
- (c) removing unbound material from the ligand; and
- (d) eluting the bound HPRG-binding molecule or cells.

62. (*new*): A method for isolating or enriching from a cell mixture cells expressing a HPRG-binding site or receptor, comprising:

- (a) contacting the cell mixture with the affinity ligand of claim 55;
- (b) allowing any cells expressing the binding site or receptor to bind to the affinity ligand;
- (c) separating cells bound to the affinity ligand from unbound cells; and
- (d) removing the bound cells,

thereby isolating or enriching the HPRG binding site-expressing cells.